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# **EUROPEAN PATENT APPLICATION**

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⑤④ Open-loop control of drug infusion.

⑤⑦ A method of determining a generalised infusion rate profile for the delivery of drugs into the circulation comprising the steps of:

(a) infusing a drug at arbitrary but known rates into a group of patients for each of whom the Lean Body Mass has been determined;

(b) determining the plasma arterial concentration of the drug in each patient at a number of specific time intervals throughout each infusion period;

(c) for each patient, estimating the rates of loss of drug in each patient at a number of specific time instants by dividing the known infusion rates per Lean Body Mass of these instants by the plasma arterial concentrations of the drug at each of these instants;

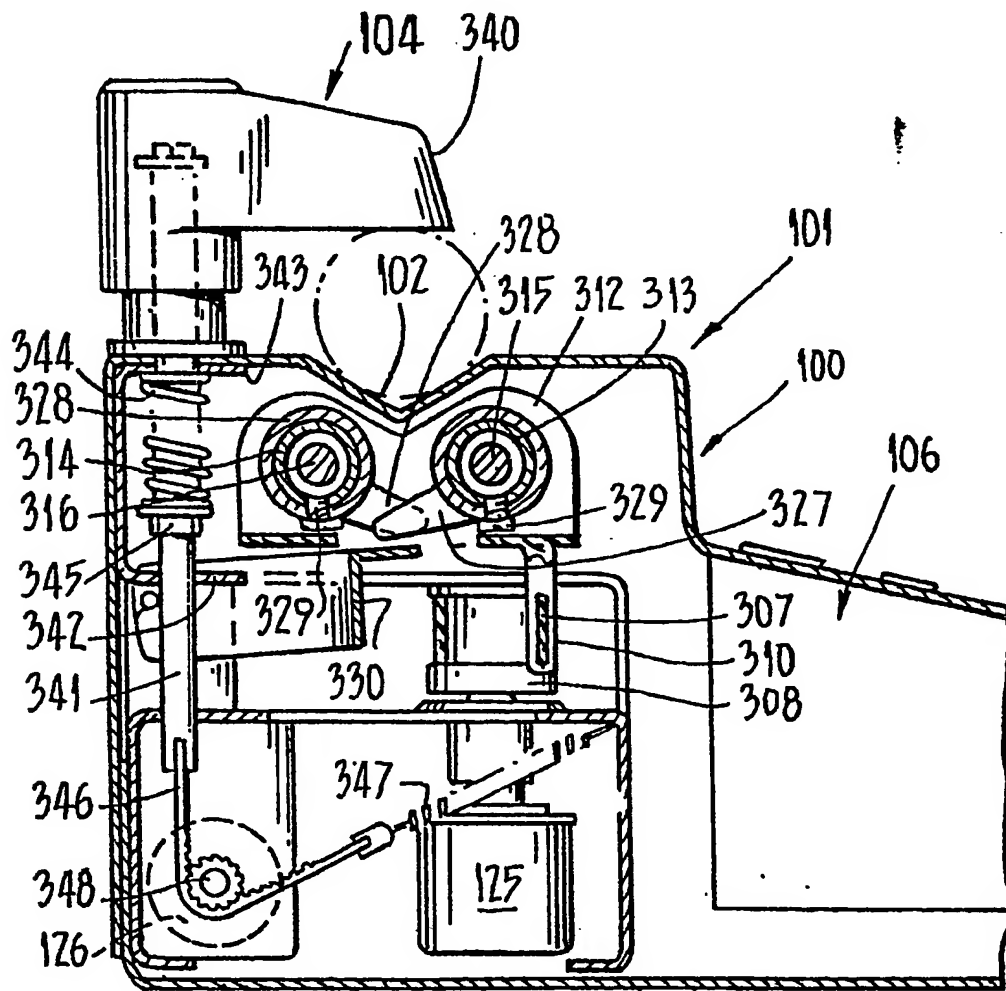
(d) calculating the average of the estimated rates of loss of drug from the circulation per Lean Body Mass unit at each specific time interval for the group of patients;

(e) interpolating the successive average points between the specific time intervals to produce an infusion profile;

(f) infusing said drug in accordance with said infusion profile determined from said interpolations into a group of patients for each of whom the Lean Body Mass has been determined, said infusion rate being scaled according to said Lean Body Mass of each patient, and

(g) repeating steps (b) to (f) until a desired steady plasma arterial content of the drug is substantially maintained throughout the infusion period.

**EP 0 164 904 A2**

FIG. 17.

1 of the drug by metabolism or excretion from the body may be  
2 obtained by:

3 
$$Cl = \text{dose/AUC}$$

4 where the plasma concentration/time curve is integrated  
5 (AUC) for up to three days following the administration of  
6 the dose of the drug, again see Gibaldi and Perrier, p 321).

7 Once the coefficients of the decay curve and the  
8 clearance of the drug have been determined, it then becomes  
9 possible using mathematical transforms to create a  
10 mathematical model which simulates the distribution and  
11 elimination of the single dose of the drug. The model  
12 consists of compartments described in terms of their volume  
13 (eg. V1, V2 and V3) and rate constants (eg. k12, k21, k13, k31  
14 and k10) for the movement of drug to and fro between the  
15 compartments (see Figure 2). The loss of drug from the  
16 system by detoxification or excretion being described either  
17 by an elimination rate constant or by the clearance of the  
18 drug from the particular patient. Such methods are fully  
19 described in many texts, particularly by Gibaldi and Perrier  
20 at pp45-111.

21 Once such a mathematical model of the subject has been  
22 created it then becomes possible to design infusion patterns  
23 in an attempt to achieve a steady concentration.

24 Earliest methods of infusion have involved the  
25 injection of a single dose of the drug followed by a  
26 constant rate infusion. The infusion is used to counteract  
27 loss of drug by elimination while the single dose, based on  
28 the amount of drug required either, to reach the desired  
29 concentration in the initial volume of distribution (V1 in  
30 Figure 2) or in the steady state volume of distribution (V1  
31 + V2 + V3 in Figure 2), is used to establish an initial  
32 concentration. Both these methods however ignore the time  
33 related movement of drug between the compartments and have  
34 proved unsatisfactory for a many drugs, particularly  
35 anaesthetic drugs which are lost rapidly from the  
36 circulation. The situation is compounded further for many  
37 anaesthetic drugs as they have very narrow ranges of safety  
38 making it highly desirable to hold concentrations close to

1 that desired by the operator.

2 Various approaches have been described in an attempt to  
3 overcome the problem of rapid loss of drug to the tissues  
4 and the consequent, highly undesirable, fluctuations in  
5 blood concentration. Some involve either substitution of a  
6 short term loading infusion for the initial bolus or  
7 alternatively the addition of a smaller loading infusion to  
8 the bolus and maintenance doses.

9 The most popular methods of infusion, however, utilize  
10 the coefficients of the compartmental model (Figure 2)  
11 derived using the methods outlined above and averaged for a  
12 number of patients to derive exponential infusions. The  
13 parameters of the model are used as a basis for calculating  
14 an infusion profile which will keep the concentration  
15 constant in the central compartment of the model on the  
16 assumption that the patient will behave as the model. Such  
17 a method results in a mono- or polyexponentially decaying  
18 infusion profile asymptoting to a constant rate which  
19 relates to the anticipated constant rate of elimination of  
20 the drug at a steady plasma concentration. The constant  
21 rate (assymptote) varies considerably between drugs, being  
22 determined by the ability of the patient to detoxify or  
23 excrete the drug. Such methods combining bolus, exponential  
24 decaying infusion and maintenance rate infusion have been  
25 described in theory by Kruger-Thiemer, E. in "Continuous  
26 intravenous infusion and multicompartment accumulation" in  
27 European Journal of Pharmacology, pp 317-324, Volume 4,  
28 (1968) and by Vaughan, DP and Tucker, GT. in "General  
29 derivation of the ideal intravenous drug input required to  
30 achieve and maintain a constant plasma drug concentration.  
31 Theoretical application to lignocaine therapy." in European  
32 Journal of Clinical Pharmacology, pp 433-440, Volume 10,  
33 1976.

34 A practical use of the exponential method, in  
35 particular the use of a computer to perform the required  
36 transforms and control the rate of a drug delivery device,  
37 has been described by Schwilden H., Schuttler J., Stoeckel  
38 H.G. and Lauven P.M. in "Strategies of Infusion for

1 Intravenous Anaesthesia" in Pharmacological Basis of  
2 Anesthesiology, eds Tiengo M. and Cousins M.J., Raven Press,  
3 1983. These authors describe a method where it is necessary  
4 to store in the memory of a computer averaged kinetic data,  
5 ie. the compartmental parameters shown in Figure 2, for  
6 each drug as well as appropriate programs to perform the  
7 considerable mathematical operations required. Then, prior  
8 to an infusion, the operator nominates the concentration  
9 required in the plasma of the subject. Then by a method, of  
10 the type described by Kruger-Theimer, an infusion pattern is  
11 computed as time passes, the magnitude of which is used to  
12 control the rate of a drug delivery device.

13 Various other approaches to the generation of  
14 exponential infusions have been described which use  
15 pneumatic or electrical means. One such method is described  
16 by Stoffregen (German Patent Application DE 3227518 A1 - 24  
17 July, 1981) which produces a mono-exponential decay. This  
18 method while apparently novel in electronic technique uses  
19 the well known exponential method and further does not  
20 appear to offer any means of generating a polyexponential  
21 decay. Also the method does not describe any means of  
22 adapting the infusion rate to achieve a nominated arterial  
23 plasma concentration of the drug or to vary the base rate of  
24 infusion in accordance with rate of elimination of the  
25 particular drug in use.

#### 26 SUMMARY OF THE INVENTION

27 The present invention recognizes:-

- 28 (i) that conditions following a single dose, by comparison  
29 with those during an infusion may well be different,  
30 particularly for drugs that have a significant effect on the  
31 rate of flow of blood through the heart and to the various  
32 organs of the body,  
33 (ii) that conditions of drug distribution and elimination  
34 are unlikely to be the same during an infusion at  
35 therapeutic levels as they are during the hours and days  
36 following a single dose,  
37 (iii) that therapeutic levels of a drug may affect the  
38 distribution of a drug to the various tissues, particularly

1 those where detoxification occurs,

2 (iv) that single dose drug elimination curves may be quite  
3 inaccurate at the extreme ends so that the early part  
4 suffers because of extrapolation and the later part because  
5 of the extremely low drug levels involved which lead to  
6 errors in the assay,

7 (v) that time related changes in the circulation may occur  
8 resulting in corresponding changes with time of the  
9 parameters of the kinetic model,

10 (vi) that drugs which produce unconsciousness cause falling  
11 levels of adrenaline and other substances which in turn  
12 alter circulatory and metabolic function, and

13 (vii) that for an infusion to be applicable to a wide  
14 variety of subjects and to be able to achieve a nominated  
15 level of the drug in a subject, some formal method is  
16 required to relate drug delivery to a measurable physical  
17 parameter which is widely applicable to subjects of varying  
18 age and morphology.

19 Central to the approach used in this method is the  
20 development of a new concept in pharmacokinetics, the Plasma  
21 Drug Efflux. This concept simply stated is that at any  
22 instant, if the plasma concentration of a drug is neither  
23 rising nor falling, the rate of delivery of the drug to the  
24 circulation ie. the infusion rate, must equate to the rate  
25 at which the drug is being lost from the circulation. It  
26 being unimportant whether the loss, is by distribution,  
27 metabolism or excretion.

28 If, by way of illustration, the blood plasma is  
29 represented as a single compartment of undetermined volume  
30 the infusion scheme may be represented as shown in Figure 3.  
31 Then if drug is administered by some arbitrary infusion  
32 scheme  $\bar{Q}(t)$ , the plasma concentration is  $C(t)$  and the rate  
33 of drug loss from the plasma may be called the Plasma Drug  
34 Efflux,  $E_p(t)$ .

35 If the plasma drug concentration is constant so that  
36 the amount of drug is not changing then the instantaneous  
37 rate of drug influx to the plasma (the infusion rate), and  
38 the instantaneous concentration in the plasma may be used as



1 an estimate of drug efflux from the plasma, is an estimate  
2 of i.e.:

3 
$$E_p \approx Q_I / C_I$$

4 The efflux estimate may then be plotted against time,  
5 and will essentially describe a dosing-rate/concentration  
6 profile as a function of time which will result in a plateau  
7 concentration for all time.

8 In practice in applying this method it is not possible  
9 at first to achieve a constant plasma concentration as this  
10 is, of course, the goal of the method. But it is possible  
11 by the use of very few iterations to closely approach this  
12 goal.

13 Thus, according to the first aspects, the present  
14 invention provides a method of determining a generalised  
15 infusion rate profile for the delivery of drugs into the  
16 circulation comprising the steps of:

- 17 (a) infusing a drug at arbitrary but known rates into a  
18 group of patients for each of whom the Lean Body Mass has  
19 been determined;  
20 (b) determining the plasma arterial concentration of the  
21 drug in each patient at a number of specific time intervals  
22 throughout each infusion period;  
23 (c) For each patient, estimating the rates of loss of drug  
24 from the circulation at a number of specific time instants  
25 by dividing the known infusion rates per Lean Body Mass at  
26 these instants by the plasma arterial concentrations of the  
27 drug at each of these instants.  
28 (d) calculating the average of the estimated rates of loss  
29 of drug from the circulation per Lean Body Mass unit at each  
30 specific time interval for the group of patients;  
31 (e) interpolating the successive average points between the  
32 specific time intervals to produce an infusion profile;  
33 (f) infusing said drug in accordance with said infusion  
34 profile determined from said interpolations into a group of  
35 patients for each of whom the Lean Body Mass has been  
36 determined, said infusion rate being scaled according to  
37 said Lean Body Mass of each patient, and  
38 (g) repeating steps (b) to (f) until a desired steady

1 plasma arterial content of the drug is substantially  
2 maintained throughout the infusion period. It must be  
3 emphasized that the shape of each infusion profile, except  
4 for the first in the series, can be determined entirely by  
5 the results obtained from the previous infusion group and  
6 that no mathematical function is assigned or required by the  
7 method.

8 The invention also provides a method of infusion of a  
9 drug into a patient comprising the steps of:

- 10 (i) determining the Lean Body Mass of the patient;
- 11 (ii) selecting a predetermined profile for the rate of  
12 delivery of drug, which rate varies with time and is  
13 configured to maintain a selected substantially steady  
14 plasma arterial content of the drug in the patient  
15 throughout an infusion period;
- 16 (iii) scaling said predetermined profile by the  
17 determined Lean Body Mass of the patient and by the desired  
18 substantially level arterial plasma concentration of drug to  
19 be maintained in the system of the patient, and
- 20 (iv) administering the drug to the patient in accordance  
21 with said scaled profile by means of an infusion device  
22 which is controlled to deliver said drug at said scaled  
23 infusion rate profile.

24 Still further the invention provides a system for  
25 achieving the method of infusion comprising an infusion  
26 system for regulating the delivery of a drug to a patient,  
27 including control means for controlling the operation of an  
28 infusion pump, said control means including pre programmed  
29 means for varying the infusion rate with respect to elapsed  
30 time, said pre programmed means varying the infusion rate in  
31 accordance with a profile which varies with time and which  
32 is adapted to maintain a desired substantially steady plasma  
33 arterial content of the drug throughout the infusion period,  
34 and operator adjustable scaling means for setting the  
35 desired concentration of said drug in the patient and for  
36 setting the Lean Body Mass of the patient, said scaling  
37 means causing modification of the pre programmed infusion  
38 rate by a fixed proportion over each time period of

1 operation of said infusion pump.

2 The invention also provides an infusion apparatus by  
3 means of which the method and system may be realised,  
4 comprising an infusion pump comprising means for receiving a  
5 syringe containing a fluid to be administered, syringe  
6 actuator means and means for driving said actuator means to  
7 move the plunger of said syringe to deliver fluid therefrom,  
8 characterised in that said drive means includes a  
9 permanently maintained connection between said drive means  
10 and a position sensing device by means of which the position  
11 of said actuator means is monitored at all times.

12 BRIEF DESCRIPTION OF THE DRAWINGS

13 A preferred embodiment of each aspect of the invention  
14 will now be described with reference to the accompanying  
15 drawings in which:

16 Fig. 1 is a graph showing the basis of prior art  
17 methods of infusion;

18 Fig. 2 is a diagram showing the basis of the  
19 compartmental model of drug distribution and elimination;

20 Fig. 3 is a diagram illustrating one model explaining  
21 the basis of the method of the present invention;

22 Fig. 4 is a graph showing the Plasma Drug Efflux data  
23 of a first group of patients to the drug thiopentone  
24 (thiopental);

25 Fig. 5 is a graph showing the average of the data point  
26 in Fig. 4 interpolated to produce an Efflux profile;

27 Fig. 6 is a graph showing the Efflux profile (b) after  
28 two iterations and the profile (a) based on the Kruger-  
29 Thiemer method;

30 Figs. 7 and 8 are graphs showing the infusion rates  
31 required for patients of indicated Lean Body Mass (LBM) and  
32 for different desired plasma concentrations for a single  
33 LBM;

34 Fig. 9 is the Plasma Efflux a profile for methohexitone  
35 (methohexital) after three iterations;

36 Fig. 10 is a graph of the arterial plasma concentration  
37 of methohexitone in a patient showing a substantially  
38 constant level at the desired concentration for the whole

1 period;

2 Fig. 11 is a perspective view of a preferred infusion  
3 pump;

4 Fig. 12 is a plan view of the control panel of the pump  
5 of Fig. 11;

6 Fig. 13 is a block diagram of the control circuitry for  
7 the pump of Fig. 11;

8 Fig. 14 is a section front elevation of the pump of  
9 Fig. 11 taken along the line 14-14 in Fig. 11;

10 Fig. 15 is a sectional elevation taken along the line  
11 15-15 in Fig. 14;

12 Fig. 16 is a sectional plan view taken along the line  
13 16-16 in Fig. 15; and

14 Fig. 17 is a sectional end elevation taken along the  
15 line 17-17 in Fig. 14.

16 DESCRIPTION OF PREFERRED EMBODIMENTS

17 Describing first the preferred method of defining a  
18 generalised infusion rate profile as applied to anaesthetic  
19 drugs, the method comprises the steps of:

20 (a) first determining the lean body mass (LBM) of a group  
21 of subjects. A convenient way of doing this in human  
22 subjects is to use the method described by Hallynck T.H. et  
23 al in "Should clearance be normalized to body surface or to  
24 lean body mass?" in British Journal of Clinical  
25 Pharmacology, p 523-526, Volume 11, (1981), who presented  
26 the following formulae:-

27 Males:  $LBM = 1.10 \times \text{weight} - 128 \times (\text{weight}^2 / \text{height}^2)$

28 Females:  $LBM = 1.07 \times \text{weight} - 148 \times (\text{weight}^2 / \text{height}^2)$

29 (b) Following administration of a suitable bolus dose of a  
30 desired drug to achieve unconsciousness, the drug is infused  
31 at an arbitrary but known rate throughout the infusion.  
32 This arbitrary infusion can be a constant rate infusion, a  
33 stepped rate infusion, an infusion pattern derived using the  
34 compartmental (Kruger-Thiemer) technique described above or  
35 an infusion pattern derived by the present method for a  
36 different drug which is known to have similar properties to  
37 the drug under test.

38 (c) From this initial set of results and by knowing the rate

1 of infusion throughout, whatever the pattern, as well as the  
2 sex, height and weight of each patient a set of data points  
3 can be obtained relating the infusion rate to the plasma  
4 arterial concentration at various times (Figure 4).

5 (d) By averaging the amplitude of the data points within  
6 specific time periods and interpolating the resulting points  
7 (Figure 5) an estimate of the Plasma Drug Efflux profile is  
8 thus obtained.

9 This estimate of the Efflux, expressed in terms of  
10 millilitres of blood cleared of drug per minute per kilogram  
11 lean body mass thus becomes the prescription for the  
12 infusion profile for the next group of subjects.

13 (e) Then by using the same method of dosing but now  
14 applying the dosage in terms of the estimated Efflux of the  
15 drug and the LBM, plasma concentrations will approach a  
16 constant and desired level without any intervention on the  
17 part of the operator.

18 (f) Iterations of this method may then be repeated three or  
19 four times if further precision is needed.

20 This is thus a new infusion profile which completely  
21 bypasses the conventional, single dose derived compartmental  
22 model described earlier in this specification. In doing  
23 this, a definition of the error for infusion dosing based on  
24 the conventional approach is also achieved. The rate  
25 profile is now derived under actual infusion dosing  
26 conditions, and is clearly a more valid approximation to the  
27 ideal infusion function.

28 Figure 6 presents a comparison between the curve of  
29 anaesthetic agent thiopentone (thiopental) for a  
30 conventional infusion rate function, based on the method of  
31 Kruger-Thiemer labelled (a), with the derived Plasma Efflux  
32 profile after two iterations normalized for plasma level,  
33 and based on actual infusion data, labelled (b).

34 A comparison of the curves shown in Figure 6 reveals:

35 (i) the rate of the new profile is much higher than the  
36 previous curve as time progresses.

37 (ii) the new profile is 10 to 20% higher in the early phases  
38 than the previous curve.

(iii) the new profile is around 50-100% higher than the old curve from about 30 minutes onwards.

The initial high level of the new profile indicates that a much higher initial infusion rate is required, quickly forcing the plasma concentration to the required level, then a rate which is about twice the conventional rate, thus holding the plasma concentration at the desired level and indicating the marked difference in the circulation during this period from that predicted by the Kruger-Theimer method.

It must be appreciated that an infusion rate that is half that actually required to achieve the desired level will result in approximately half the arterial plasma concentration during that period of the infusion.

As stated above, some drugs, particularly those used in anaesthesia, must be used within a narrow range of concentrations. If, for example, the concentration of methohexitone (Fig. 10) moves from a normally desired level of 4 to 6 mg/l to 10 mg/l the severe depression of the heart and breathing may occur while a fall to below 3 mg/l is likely to result in wakening of the patient.

As described above the plasma drug efflux profile presented in Figure 6 is normalized to unit plasma concentration and unit patient lean body mass.

In order to apply the data presented in Figure 6 to a practical infusion device, it is necessary to multiply the amplitude of the plasma drug efflux curve first by a numerical value representing the size of the patient (Lean Body Mass), and secondly, by a numerical value representing the actual plasma concentration of the drug required by the operator.

Figure 7 shows the actual infusion rate required for applying the curve of Fig. 6 curve (b) to patients of 20, 40, 60 and 80 kg LBM in order to achieve a steady plasma concentration of 1 mg/l of thiopentone. It can be seen that the shape of the generalized profile for plasma drug efflux remains the same as presented in Figure 6 curve (b) but that the magnitude is altered throughout the profile in direct

1 proportion to the Lean Body Mass of the patient.

2 Figure 8. demonstrates a further scaling operation of  
3 the curve of Figure 6 curve (b) where the actual infusion  
4 rates required for a 50 kg LBM patient, in order to achieve  
5 steady plasma concentrations of 1, 5, 10 and 20 mg/l are  
6 presented.

7 It is of interest to note that in a further application  
8 of the technique of the invention to the anaesthetic agent  
9 methohexitone (methohexital) (Figure 9) that the Plasma Drug  
10 Efflux profile, derived from actual infusion data, for this  
11 drug after three iterations bears little relationship to an  
12 exponential function, having two distinct humps. It is of  
13 further interest to note that an application of the Efflux  
14 profile of Figure 9 to generate an infusion in a typical  
15 patient (Figure 10) has resulted constant and desired  
16 arterial plasma drug concentrations over a period of five  
17 hours. The broken line in the Figure indicates the  
18 concentration desired by the operator. Similar results have  
19 been achieved on many patients with no material departures  
20 from the desired level in any patient.

21 It will be appreciated that the above method may be  
22 used to derive similar Plasma Drug Efflux profiles for other  
23 anaesthetic agents and for other drugs where a desired level  
24 of the drug in the system of the patient is to be maintained  
25 over an extended period of time.

26 While the most commonly used intravenous anaesthetic  
27 agents, thiopentone and methotexitone, have been used as  
28 examples, the methods, and the apparatus to be described  
29 below, are equally applicable to the administration of all  
30 intravenous anaesthetic agents including propofol, diazepam,  
31 midazolam and etomidate, as well as narcotic analgesics  
32 including morphine, pethidine, alfentanil, sufentanil,  
33 fentanyl and phenoperidine.

34 It will be appreciated from the above that the Efflux  
35 profile may be used to control a programmable infusion pump  
36 so that a selected drug may be delivered to a patient in  
37 accordance with the profile, as scaled by the Lean Body Mass  
38 of the patient and level of the drug desired by the operator

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1 to be maintained in the system of the patient. The profile  
2 is most suitably programmed into a device capable of  
3 controlling the infusion pump and since a different profile  
4 is required for each drug, this is most suitably achieved by  
5 the use of a programmed module which is inserted by the  
6 operator into the infusion pump controller circuit. One  
7 preferred embodiment of such an infusion pump will now be  
8 described.

9 By using the average rate of loss of the drug among  
10 different subjects against time an infusion pattern is  
11 produced which approaches the optimal pattern. This new  
12 pattern may then be applied to the next group of patients so  
13 that an iterative process results whereby an optimized curve  
14 is produced.

15 Referring now to Figs. 11 to 17, a preferred embodiment  
16 of the infusion pump for performing the drug infusion method  
17 and its control circuitry is shown. The infusion pump will  
18 be seen to comprise a casing 100 within which the syringe  
19 drive and other mechanisms described below are located. the  
20 casing 100 including a syringe cradle 101 having a central  
21 groove 102 for locating the body of a syringe and a slot 103  
22 for receiving and locating the syringe flange. A vertically  
23 moveable syringe holder and sizer 104 is positioned over the  
24 groove 102 and a syringe actuator 105, which is driven by  
25 the syringe drive in a manner further described below, to  
26 engage the syringe plunger to deliver fluid from the syringe  
27 at the rate determined by the syringe drive under the  
28 influence of its control circuitry.

29 The casing is also provided with a front panel 106  
30 including the required input keys and displays. The casing  
31 further includes a window 107 through which the name of the  
32 program drug appearing on a program module 108 which is  
33 inserted into a receiving cavity in the casing 100 in the  
34 direction of the arrow, may be read.

35 Referring now to Fig. 13, the front panel 106 will be  
36 seen to include 4 four digit LCD displays 109, 110, 111 and  
37 112. The first display 109 is associated with a first  
38 sector 113 of the panel 106 and includes illuminatable



1    message displays for syringe concentration, patient  
2    concentration and dose given as well as the alternative  
3    measurement displays mg, mg/ml or mg/l. Thus when the  
4    relevant displays are illuminated, the four digit display  
5    indicates the level of the illuminated parameter.

6        The second display 110 is associated with a second  
7    sector 114 of the panel 106 which relates to the syringe and  
8    the rate of infusion therefrom. The infusion rate may be  
9    displayed in ml/min or ml/h by actuating an option switch  
10   inside the casing 100. The volume in the syringe is  
11   displayed in ml.

12        The third display 111 is associated with a third sector  
13   115 which displays patient data including illuminatable  
14   displays which prompt the selection of male or female and  
15   prompt the inputting of the patients height and weight. A  
16   further option select switch is available to indicate the  
17   height of the patient in inches rather than in centimetres.

18        The fourth display 112 is associated with a fourth  
19   sector 116 which relates to elapsed time and also includes  
20   illuminatable displays indicating the status of the battery,  
21   occlusion, malfunction and operator error.

22        To the right of sector 116 a fifth panel 117 includes a  
23   key pad 118 for numeric entry including a cancelled button  
24   and an enter button. The panel 117 also includes five  
25   selection buttons selecting the functions: battery power,  
26   run, pause, reset and bolus. A battery charge level  
27   indicator 119 is also provided in the front panel 106.

28        Numeric entry into any one of the displays 109 to 112  
29   is achieved by scrolling through the data displays using the  
30   set button associated with the relevant panel sector 113 to  
31   116 followed by entry of the value by means of the key pad  
32   118. Once the desired value is displayed, the operator may  
33   press the enter button so that the value is entered into the  
34   memory of the control circuitry to be described below.

35        The infusion pump is capable of operating at three  
36   levels:

37        Level 1 -    The rate of infusion is entered directly on  
38   the front panel and the pump will deliver any solution at

1 this rate only - or until the rate is manually changed.

2 Level 2 - The rate can be set by a remote device such  
3 as a computer. The Infusion Pump will communicate with the  
4 remote device by means of an isolated serial port.

5 Level 3 - The rate of delivery of certain anaesthetic  
6 drugs is determined by the EPROM module 108 which is plugged  
7 into the infusion pump casing 100. This module will vary  
8 the rate with time and the relationship between these two  
9 factors will depend on the type of drug. Consequently, a  
10 separate module will be required for each drug type.

11 The rate as read from the EPROM module 108 is  
12 normalised, and the control unit will scale this to the  
13 patients sex, weight and height. These factors are entered  
14 on a front panel keyboard as described below. A serial port  
15 (Serial I/O option - Fig. 14) is an 'add-on' option capable  
16 of operating with or without an EPROM module plugged into  
17 the unit. Once appropriate control codes are sensed at the  
18 port, the unit will assume Level 2 operation. The serial  
19 port will also be capable of acting as a printer output for  
20 Level 1 or Level 3 operation.

21 Referring now to Fig. 15 of the drawings, the control  
22 circuitry for the infusion pump will now be described.  
23 Central to the control circuitry is a micro computer 120,  
24 which in the present embodiment is a type 80C39, which  
25 operates in accordance with an operating program stored in  
26 EPROM 121. The EPROM 121 may form part of the micro  
27 processor 120, and such a micro processor is available in  
28 the form of an 80C48. The micro processor 120 controls the  
29 speed of the motor in the syringe drive to be described  
30 below via a MOSFET driver circuit 122. The voltage applied  
31 to the motor via the circuit 122 is sensed by the line 123  
32 which is connected to an analog to digital convertor 124  
33 which also receives signals from feedback potentiometers 125  
34 and 126 which respectively monitor the position of the  
35 syringe actuator 105 in Figure 14, and indicate the syringe  
36 size via movement of the syringe sizing arm 104. Each  
37 feedback potentiometer 125, 126 is preferably a ten turn 50k  
38 ohm wire wound potentiometer since such potentiometers are

1 accurate, reliable and inexpensive. An optical encoder 127,  
2 which forms part of the motor monitors the speed of the  
3 motor and feeds this data to the micro processor 120 so that  
4 the speed of the motor is accurately controlled by the micro  
5 processor 120.

6 A 6 MHz crystal clock signal generator 128 is connected  
7 to the micro processor 120 to enable the necessary timing  
8 functions to be performed. The micro processor 120 and the  
9 motor are powered by means of a battery 129 which is  
10 connected to the micro processor 120 and to the motor drive  
11 circuit 122 via a DC-DC convertor 130 which removes any  
12 unwanted variations in the battery supply voltage. A  
13 charger 131 is provided to enable the battery 129 to be  
14 recharged.

15 The micro processor 120 is also connected to a switch  
16 132 positioned on the syringe actuator 105 with closure of  
17 the switch 132 indicating that the contact between the  
18 syringe actuator 105 and the syringe plunger has occurred.  
19 The switch 132 is preferably a single pole double toggle  
20 switch which indicates not only when contact between the  
21 syringe actuator 105 and the syringe plunger has occurred  
22 but also when disengagement between the syringe actuator 105  
23 and the syringe plunger has occurred. Although this  
24 arrangement is presently preferred, it is also possible for  
25 the micro processor 120 to sense when the current drawn by  
26 the motor increases and decreases, via line 123, so that the  
27 engagement and disengagement between the syringe actuator  
28 105 and the syringe plunger may be detected.

29 The LCD displays 109 to 112 are connected to LCD driver  
30 circuits 133 while the remaining indicator lamps and LED  
31 battery charge indicator 119 are connected to lamp driver  
32 circuits 134. A warning buzzer 135 is also provided for the  
33 purpose to be described further below.

34 The operating program stored in EPROM 121 causes the  
35 infusion pump to function in the following manner.

36 At "power on" all displays are illuminated for one  
37 second and then turned off. An internal test sequence is  
38 performed in which the presence of the drug specific EPROM

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1 module is detected and any malfunction in the displays is  
2 noted and, if so, the malfunction display illuminated.  
3 Thereafter, the initialisation sequence commences in which  
4 the "syringe concentration" display is illuminated and the  
5 units in mg/ml is displayed via the display 109 taking the  
6 usual concentration of the drug read from the module 108,  
7 for example, thiopentone - 25 mg/ml, methohexitone - 10  
8 mg/ml, fentanyl - 0.050 mg/ml. The operator may then press  
9 the set button in sector 113 or perform the numeric entry  
10 sequence for a desired syringe concentration value. The  
11 resulting syringe value, whether it remains as read from the  
12 EPROM or is altered by the operator, is stored in memory to  
13 be used to scale delivery of the drug containing fluid.  
14 After entry of this data or after the set button is pressed,  
15 the "patient concentration" display is illuminated and an  
16 average value as read from the module 108 is displayed at  
17 109, for example, thiopentone 10.0 mg/l or methohexitone 5.0  
18 mg/l. The displayed value may be modified by the numeric  
19 entry sequence described above. The EPROM module 108 stores  
20 an acceptable range of patient concentrations for each drug,  
21 for example, thiopentone 5-20 mg/l and methohexitone 2-12  
22 mg/l. If values outside these ranges are entered then the  
23 'patient concentration' display is flashed in all modes of  
24 operation until the value is brought within the range. On  
25 pressing the set button or the enter button, entry to this  
26 sector is complete and the first display on the syringe  
27 sector 114 ("load empty") is illuminated.

28 The operator raises the syringe holder and sizer 104  
29 and loads an empty syringe into the syringe cradle 101 and  
30 presses the set button in sector 114. The motor is  
31 activated and the syringe drive to be described further  
32 below moves the syringe actuator 105 towards the empty  
33 syringe until closure of the switch 132 indicates contact  
34 and the position of the syringe actuator 105 is stored in  
35 the memory of the micro processor 120. This is the zero  
36 position (plunger length) of that particular syringe. The  
37 syringe diameter as detected by the syringe holder and sizer  
38 104 through feedback potentiometer 126 is also stored in the

1 memory. If no syringe is loaded, the previously stored  
2 zero position and syringe diameter are assumed and the  
3 syringe actuator 105 is driven fully to the left to await  
4 the loading of a filled syringe.

5 The "load filled" display is then illuminated and the  
6 operator loads a syringe and presses the set button. At  
7 this point, a comparison is made between the previous  
8 diameter and the new diameter and if a discrepancy of  
9 greater than  $\pm 2.5\%$  is noted, the "load empty" display is  
10 illuminated in order to calibrate for a new syringe. If the  
11 new diameter matches the old then the "volume" display is  
12 illuminated and the volume of the syringe computed from the  
13 diameter of the syringe and the displacement of the syringe  
14 actuator 105 from the zero position is displayed at 110 and  
15 stored in the memory of the infusion device in order to  
16 adapt plunger movement to deliver the required volume as  
17 determined by other calculations. As an optional safety  
18 feature, the operator may be required to enter the loaded  
19 volume of the new syringe and if the entered value differs  
20 by more than  $\pm 10\%$  of the previously computed value, the  
21 calibration procedure is recommenced from "load empty".

22 It has been found that the variation in wall thickness  
23 of commercially available syringes of similar internal  
24 diameters is insignificant when regard is had to the error  
25 tolerance in the volume of drug which may be infused into a  
26 patient as well as the acceptable error in the formulation  
27 of the drug solution. Accordingly, the diameter measurement  
28 which is made by the syringe holder and sizer 104 is  
29 sufficiently accurate to provide the necessary volume  
30 measurement during the infusion process.

31 After the filled syringe is loaded and the syringe  
32 actuator 105 is in contact with the syringe plunger, the  
33 "sex M=0 F=1" display is illuminated followed by the  
34 "height" and "weight" displays in sequence for numeric entry  
35 of the values relating to the particular patient to be  
36 treated. If the operator wishes to enter the patient height  
37 in inches, the internal switch is actuated. The operator  
38 enters these patient parameters, the Lean Body Mass is

1 calculated, displayed on display 111 and stored in the  
2 memory of the device for use in adapting infusion rates to  
3 the particular patient. Once the patient data entry is  
4 completed, the set button is pressed and the display 112  
5 will scroll through the values entered in sector 116, at  
6 which time any value may be changed by the numeric entry  
7 procedure.

8 After the patient data has been entered, all displays  
9 should be blanked except for the time which will show 00:00.  
10 At this stage, the elapsed time may be preset using the  
11 numeric entry sequence in the event that the pump needs to  
12 be restarted within an infusion sequence. The zero elapsed  
13 time or the operator preset time is indicated on display 112  
14 and stored in the memory of the device for use in  
15 determining the point to start reading the infusion pattern.

16 When the patient is ready for treatment, the run button  
17 is pressed with the elapsed time incrementing, except during  
18 activation of the pause button, and shown on display 112.  
19 The syringe display 110 will show the delivery rate in  
20 ml/min or ml/h if the option switch has been actuated. The  
21 patient display 111 indicates the Lean Body Mass of the  
22 patient in kg calculated by the formula referred to above.  
23 The drug display 109 indicates the accumulated dose of drug  
24 administered to the patient.

25 Whenever the pause button is pressed, the time clock  
26 stops operation and the syringe display 110 indicates the  
27 total volume delivered since commencement of operation and  
28 the volume display is illuminated. The patient display  
29 remains unaltered while the drug display 109 indicates the  
30 dose given since the previous reset or commencement, the  
31 dose given display being illuminated at the same time.

32 It should be emphasised that by virtue of the syringe sizing  
33 mechanism and the plunger sensing switch of the device the  
34 accumulated volume and doses displayed will represent the  
35 sum of all syringes loaded whatever the volume or size of  
36 syringe used. Change of any display can occur at this point  
37 by pressing the appropriate set button and if the syringe  
38 holder and sizer 104 is lifted or the syringe actuator 105

1 is moved, the syringe sequence recommences at the "load  
2 filled" point.

3 If the bolus button is pressed at any time, the syringe  
4 and drug displays are immediately zeroed and drug delivery  
5 commences at a rate of the order of 1 ml/sec for a 50 ml  
6 syringe, the display "dose given" is illuminated and the  
7 progressive volume delivered is displayed at 110 in ml. On  
8 release of the bolus button, the syringe display reverts to  
9 a display of the running rate, the drug display 109 shows  
10 the sum of the bolus and the previous dose while the time  
11 display reverts to the previous mode.

12 Pressing the BAT button causes illumination of the LED  
13 display 119 to indicate the condition of the battery.

14 If either the syringe switch 132 or the syringe holder  
15 and sizer 104 is moved to a new position for more than two  
16 seconds, the syringe actuator 105 is driven to the left and  
17 the syringe set sequence is recommenced at the "load filled"  
18 point. If an occlusion is detected by a sudden increase in  
19 the drive current to the motor, via line 123, the syringe  
20 actuator 105 is driven to the left until the switch 132 is  
21 disengaged, whereupon the "occlusion" display is illuminated  
22 and the buzzer 135 actuated. The detection of occlusion is  
23 related to a diameter of the syringe, detected by the  
24 syringe sizing mechanism so that the larger drive current  
25 required for larger syringes will not cause a false  
26 occlusion alarm. One way of achieving this is to store data  
27 relating to the maximum force required to move a syringe at  
28 various rates in use and to scale this force in accordance  
29 with the detected diameter.

30 Occlusion of the drug delivering conduit by a tap  
31 represents considerable danger to a patient if a highly  
32 potent drug is contained in the syringe and the tap is  
33 suddenly opened while under pressure. The three features of  
34 adjusting occlusion pressure detection to the measured  
35 syringe diameter, backing of the drive once overpressure is  
36 detected and sounding the alarm after the pressure is  
37 removed are specifically designed to lessen this risk.

38 Illumination of the "malfunction" display occurs

1 whenever any form of malfunction is identified and the  
2 buzzer 135 is actuated. Similarly, the "operator error"  
3 display will be illuminated in the event of an operator  
4 error being detected, such as, pushing forward manually on  
5 the drive mechanism when the drive mechanism is connected or  
6 the entry of incompatible syringe sizes for a given LBM.  
7 Syringe to patient incompatibility is determined by  
8 calculating the ratio of the Lean Body Mass of the patient  
9 to the sensed diameter of the syringe and relating this  
10 ratio to the rate fluid is to be delivered. It being  
11 recognized that considerable inaccuracy will result if a  
12 very large syringe is used with a very small patient.

13 As mentioned above, three levels of operation may be  
14 selected and the level of operation determines the rate at  
15 which the fluid in the syringe is delivered and this rate  
16 continues, as programmed, unless any one of the following  
17 occurs:

18 the bolus key is depressed.

19 an occlusion occurs.

20 a system malfunction occurs.

21 the plunger is manually pushed forward to administer  
22 more fluid (as sensed by the plunger position potentiometer  
23 125). The switch 132 shows the plunger is disengaged.

24 the syringe size potentiometer 126 indicates a change  
25 in reading, or

26 the pause key is pressed.

27 In Level 3 operation, an infusion pattern stored in the  
28 EPROM 108 is followed by the infusion pump. The pattern is  
29 drug dependent and a separate module 108 is used for each  
30 type of drug. Typical infusion patterns for thiopentone and  
31 methohexitone are shown in Figs. 6 and 9 of the drawings and  
32 are described in greater detail above. The rate of drug  
33 delivery stored in the module 108 is scaled by the Lean Body  
34 Mass data entered in the manner described above as well as  
35 by the desired concentration data entered by the operator.  
36 The effect of this scaling is clearly shown in Figs. 7 and 8  
37 of the drawings which indicate drug delivery rate in terms  
38 of the dose delivered per minute. The volume of drug



1 containing fluid which must be delivered is further scaled  
2 in accordance with usual concentration of the particular  
3 drug in the syringe which is read from the drug specific  
4 EPROM 108 or entered by the operator during the  
5 initialization sequence. Then using the result of these  
6 previous calculations the actual movement of the syringe  
7 actuator is scaled in proportion to the syringe diameter as  
8 determined by the syringe sizing mechanism.

9 During Level 3 operation, a bolus is automatically  
10 administered at time 00:00 unless the operator indicates,  
11 via keyboard input, that a bolus has been previously  
12 administered.

13 This starting bolus is administered at a rate  
14 determined by data stored in the EPROM module 108, the  
15 volume administered being scaled according to the entered  
16 Lean Body Mass desired concentration and the concentration  
17 of drug in the syringe. The amount delivered is displayed  
18 at 109 with the "dose given" display illuminated.

19 During normal operation additional drug may be  
20 administered by pressing the bolus key and will continue at  
21 the rate described above for as long as the key is  
22 depressed.

23 Referring now to Figs. 14 to 17 of the drawings, the  
24 syringe drive mechanism will now be described in greater  
25 detail.

26 The drive motor M is preferably an ESCAP DC gear motor  
27 type MA1616 C11 with 243:1 gear ratio and B type optical  
28 encoder. The output shaft of motor M is fitted with a  
29 toothed or knurled drive wheel 300 and the motor is mounted  
30 on a pivoted arm 301 (Fig. 16) which is pivoted towards its  
31 "drive engaged" position under the influence of a spring  
32 302. The drive wheel 300 engages a polyurethane drive ring  
33 303 which encircles a driven wheel 304 which transmits drive  
34 through a shaft 305 to a toothed drive head 306. A toothed  
35 drive belt 307 engages the drive head 306 and also passes  
36 around a similar toothed drive head 308 spaced from the  
37 drive head 306 at the opposite end of the casing 100. Both  
38 drive heads 306, 308 are mounted in bearings on a frame 309

1 and the drive head 308 is drivingly connected to the  
2 position feedback potentiometer 125 which is supported below  
3 the frame 309 in the manner shown (Fig. 14). It should be  
4 appreciated that the belt drive may be replaced by a chain  
5 or similar flexible drive although the belt drive is  
6 preferred for practical reasons.

7 A permanent driving connection is effected between the  
8 drive belt 307 and the syringe actuator 105 by means of belt  
9 clamp 310 having a connector plate 311 which is in turn  
10 attached to a slider 312 which is connected to the syringe  
11 actuator 105 by means of tubes 313, 314 surrounding a pair  
12 of spaced parallel guide rods 315, 316 which extend  
13 longitudinally of the casing 100 and into the syringe cradle  
14 101. Both the slider 312 and the syringe actuator 105 are  
15 provided with bearings 317, 318 which engage the guide rods  
16 315, 316 to facilitate sliding movement of the slider 312  
17 and the syringe actuator 105. The tubes 313, 314 engage  
18 seals 319 in the syringe cradle 101 to prevent ingress of  
19 foreign matter into the casing 100.

20 It will be appreciated from the above that a permanent  
21 driving connection is maintained between the belt 307 and  
22 the syringe actuator 105 so that the position potentiometer  
23 125 is at all times able to accurately sense the position of  
24 the syringe actuator 105. In other words, there is not in  
25 the present embodiment of the invention, as in some prior  
26 art infusion pumps, the ability to disconnect the drive  
27 between the syringe actuator and the driving mechanism.  
28 However, it is possible to disengage the drive wheel 300  
29 from the driven wheel 304 to enable easy manual movement of  
30 the syringe actuator 105 during loading and unloading of a  
31 syringe.

32 In the present embodiment, drive release is achieved by  
33 manually depressing push buttons 320, 321 mounted in the  
34 syringe actuator 105. The buttons 320, 321 extend from the  
35 ends of arms 322, 323 which in turn extend from mounting  
36 sleeves 324, 325 which surround the tubes 313, 314 and are  
37 fixed to impart rotation thereto by means of grub screws 326  
38 when the buttons 320, 321 are depressed. It will be

1 appreciated from the above that the tubes 313, 314 are free  
2 to rotate in both the syringe actuator 105 and the slider  
3 312.

4 Drive release actuating cams 327, 328 are attached to  
5 tubes 313, 314 by means of grub screws 329 and are located  
6 within the slider 312. The cams 327, 328 are positioned to  
7 contact a motor release bar 330 (Figs. 16 and 18) which is  
8 in the form of a bell-crank lever having its pivot extending  
9 longitudinally of the casing 100. The other arm 331 of the  
10 bell-crank lever is attached by a link 332 (Figs. 16 and 17)  
11 to the pivoted motor mounting plate 301. Thus by depressing  
12 the buttons 320, 321, with one hand, the tubes 313, 314 are  
13 rotated to bring the cams 327, 328 into contact with the  
14 motor release bar 330 which pivots the plate 301 to the left  
15 in Fig. 17 to move the drive wheel 300 out of engagement  
16 with the rim 303 of the driven wheel 304. When thus  
17 released, the syringe actuator 105 may be freely moved along  
18 the guide rods 315, 316 although by virtue of the permanent  
19 connection to the drive belt 307, the position sensing  
20 potentiometer 125 continues to register the position of the  
21 syringe actuator 105 at all times.

22 It will be appreciated that motor release may be  
23 achieved with only one button and associated tube and cam  
24 mechanism.

25 Referring now to Figs. 14 and 17, the syringe holder  
26 and sizer 104 will be seen to comprise a clamping arm 340  
27 mounted on a vertically extending shaft 341 supported for  
28 vertical sliding movement by frame members 342, 343 and  
29 biased towards a clamping position by means of compression  
30 spring 344 engaging a flange retainer 345 attached to the  
31 shaft 341. At its lower most end, the shaft 341 has an  
32 element of toothed drive belt 346 attached thereto and a  
33 light biasing spring 347 is attached to the other end of the  
34 belt 346 to maintain it in engagement with a gear wheel 348  
35 keyed to the shaft of the syringe sizing potentiometer 126.  
36 In this way the syringe holder and sizer 104 operates to  
37 clamp the syringe in the syringe cradle 101 and causes the  
38 sizing potentiometer 126 to transmit a syringe size signal

1 to the micro processor 120 via the analog to digital  
2 convertor 124.

3 The rating of the spring 302 is selected so that the  
4 driving gear 300 will slip on the rim 303 of the driven  
5 wheel 304 in the event that a severe occlusion occurs and  
6 the syringe plunger does not move into the syringe. Of  
7 course in most instances, the micro processor 120 will sense  
8 an excessive increase in motor current and will stop the  
9 motor M.

1 What the claim is:

2 1. A method of determining a generalised infusion rate  
3 profile for the delivery of drugs into the circulation  
4 comprising the steps of:

5 (a) infusing a drug at arbitrary but known rates into a  
6 group of patients for each of whom the Lean Body Mass has  
7 been determined;

8 (b) determining the plasma arterial concentration of the  
9 drug in each patient at a number of specific time intervals  
10 throughout each infusion period;

11 (c) for each patient, estimating the rates of loss of drug  
12 from the circulation at a number of specific time instants  
13 by dividing the known infusion rates per Lean Body Mass of  
14 these instants by the plasma arterial concentrations of the  
15 drug at each of these instants;

16 (d) calculating the average of the estimated rates of loss  
17 of drug from the circulation per Lean Body Mass unit at each  
18 specific time interval for the group of patients;

19 (e) interpolating the successive average points between the  
20 specific time intervals to produce an infusion profile;

21 (f) infusing said drug in accordance with said infusion  
22 profile determined from said interpolations into a group of  
23 patients for each of whom the Lean Body Mass has been  
24 determined, said infusion rate being scaled according to  
25 said Lean Body Mass of each patient, and

26 (g) repeating steps (b) to (f) until a desired steady  
27 plasma arterial content of the drug is substantially  
28 maintained throughout the infusion period.

29 2. The method of Claim 1, wherein said drug is an  
30 anaesthetic agent and each patient in each group is first  
31 given a bolus dose of said drug sufficient to produce an  
32 appropriate initial arterial blood concentration.

33 3. The method of Claim 2, wherein said initial  
34 predetermined rate of infusion is selected from a constant  
35 rate infusion, a step rate infusion, an infusion profile  
36 derived using the Kruger-Theimer Compartmental Model, and an  
37 infusion pattern derived by the method according to Claim 1  
38 for a different drug which is known to have properties

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1 8. The system of Claim 7, wherein said pre programmed  
2 means comprises a read only memory module containing said  
3 profile relating to the drug to be administered, said  
4 control means including a port for receiving said module.

5 9. The system of Claim 7 or Claim 8, including operator  
6 adjustable sealing means for setting the concentration of  
7 said drug in a fluid containing said drug.

8 10.\* The system of Claim 8, wherein said preprogrammed read  
9 only memory module contains information related to the drug  
10 to be delivered, including the usually prescribed  
11 concentration of the drug in a fluid containing such drug,  
12 an average plasma concentration for achieving an effect in  
13 the patient with the drug and an acceptable range of plasma  
14 concentrations of the drug.

15 11. An infusion pump comprising means for receiving a  
16 syringe containing a drug containing fluid to be  
17 administered, syringe actuator means and means for driving  
18 said actuator means to move the plunger of said syringe to  
19 deliver fluid therefrom, characterised in that said drive  
20 means includes a permanently maintained connection between  
21 said drive means and a position sensing device by means of  
22 which the position of said actuator means is monitored at  
23 all times.

24 12. The pump of Claim 11, wherein said drive means  
25 comprises a motor and a drive train driven by said motor,  
26 said drive train including said permanently maintained  
27 connection, and means for disconnecting drive between said  
28 motor and said drive train to enable said actuator means to  
29 be freely moved whilst maintaining said permanent connection  
30 so that the position of said actuator means is monitored.

31 13. The pump of Claim 12, wherein said drive train includes  
32 a driven wheel, a driving head connected to be driven by  
33 said driven wheel, a further driving head spaced from said  
34 driving head and a flexible driving connection  
35 interconnecting said driving heads so that said further  
36 driving head is positively driven by said driving head.

37 14. The pump of Claim 13, wherein said flexible driving  
38 connection comprises a toothed belt, the teeth of which

- 1 positively engage teeth formed on said driving heads.
- 2 15. The pump of Claim 14, wherein said permanently
- 3 maintained connection comprises a plate clamped to said belt
- 4 and rigidly secured to means for moving said actuator means.
- 5 16. The pump of Claim 15, wherein said position sensing
- 6 device comprises a rotary potentiometer driven by said
- 7 further drive head, the output of said potentiometer being
- 8 connected to control circuitry for said motor whereby the
- 9 position of said actuator means is sensed.
- 10 17. The pump of Claim 12, wherein said means for
- 11 disconnecting drive between said motor and said drive train
- 12 comprises manually actuatable means on said actuator means.
- 13 18. The pump of Claim 17, wherein said means on said
- 14 actuator means comprises at least one depressible lever
- 15 which causes actuation of a further lever which disengages
- 16 said motor from said drive train.
- 17 19. The pump of Claim 18, wherein said motor is mounted on
- 18 a pivoted arm to which a bell-crank lever is connected by a
- 19 linkage said bell-crank lever being actuated by depression
- 20 of said at least one lever.
- 21 20. The pump of Claim 19, wherein said actuator means
- 22 supports two manually operable levers which are in turn
- 23 connected to tubes rotatably mounted in the actuator means
- 24 and slideably supported by guide rails, said tubes also
- 25 being rotatably mounted in a slider spaced from said
- 26 actuator means and to which said permanently maintained
- 27 connection is attached, said tubes supporting cams which
- 28 engage a motor releasing lever when said levers carried by
- 29 said actuator means are manually depressed to disengage said
- 30 motor from said drive train.
- 31 21. The infusion pump of Claim 11, further comprising a
- 32 syringe holding and sizing means in the form of a syringe
- 33 clamp to which a sizing mechanism is connected.
- 34 22. The pump of Claim 21, wherein said sizing mechanism
- 35 comprises a rotary potentiometer, the output of which is
- 36 connected to control circuitry for said pump whereby the
- 37 diameter of the syringe is automatically measured thereby
- 38 enabling the calculation of the volume of said syringe.



1 23. The pump of Claim 11, further comprising control  
2 circuitry for said pump which controls the rate of delivery  
3 of said drug containing fluid, said control circuitry  
4 including a programmable module which is pre programmed with  
5 information concerning each drug to be administered by means  
6 of said infusion pump according to a predetermined profile  
7 which varies with time and which maintains a desired  
8 substantially steady level of the drug in the patient to  
9 whom the drug containing fluid is delivered.

10 24. The pump of Claim 23, wherein said control circuitry  
11 further comprises means for scaling the programmed profile  
12 in said module in accordance with the estimated Lean Body  
13 Mass of the person, the desired level of drug to be  
14 maintained in the person.

15 25. The pump of Claim 11, further comprising a switch  
16 mounted on said actuator means and positioned to engage the  
17 plunger of a syringe supported by said pump, said switch  
18 being connected in control circuitry for said pump to  
19 indicate that the actuator means has engaged a syringe  
20 mounted on said pump.

21 26. The pump of Claim 23, wherein means is provided for  
22 varying the rate of delivery of said drug containing fluid  
23 in accordance with a variation in the concentration of the  
24 drug in the fluid.

25 27. The pump of Claim 26, wherein means is provided for  
26 entering a variation in the concentration of the drug in the  
27 fluid.

28 28. The pump of Claim 11, comprising means for displaying  
29 the quantity of drug infused.

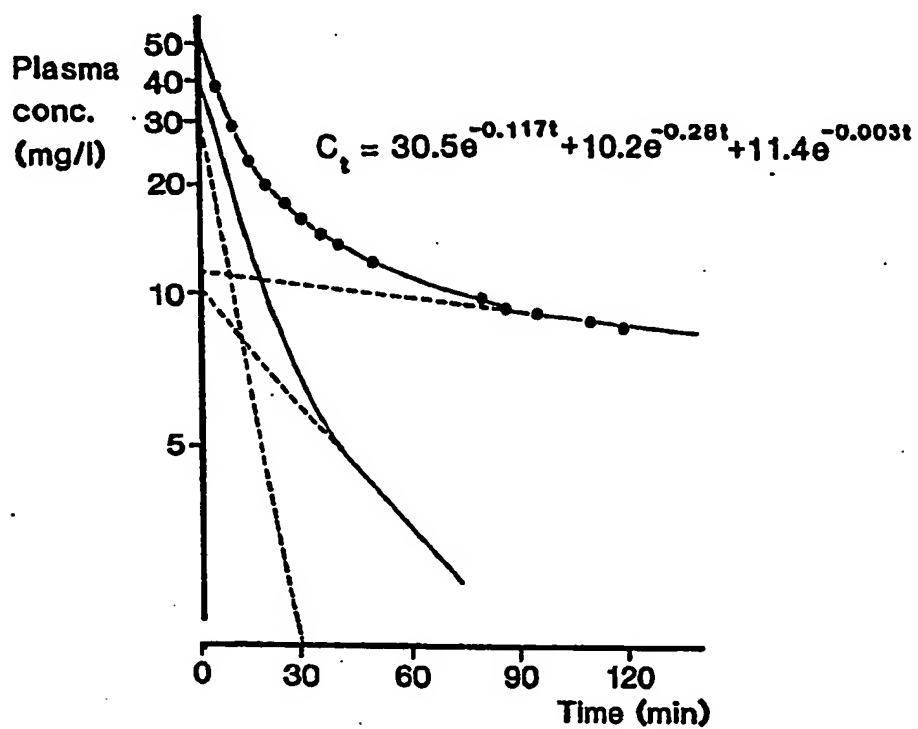
30 29. The pump of Claim 11, including means adapted to detect  
31 a pressure greater than a predetermined required to deliver  
32 fluid is detected.

33 30. The pump of Claims 22 and 29 and adapted to vary said  
34 predetermined pressure in relation to variation in syringe  
35 size.

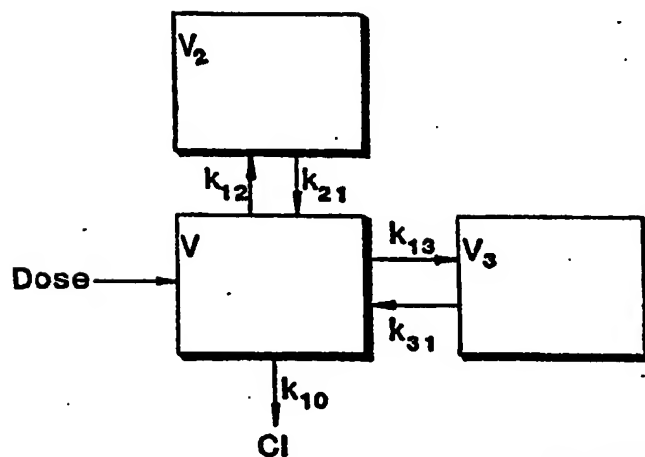
36 31. The pump of Claim 25 and 27 and adapted to determine  
37 that an overpressure has been released.

38 32. The pump of Claims 11, 22 and 25, including means for

- 1 detecting a syringe replacement, a variation and syringe
- 2 size and means adapted to store an accumulation of drug
- 3 dosage consequent on syringe replacement and/or variation of
- 4 syringe size.



III . 1 .



III . 2 .

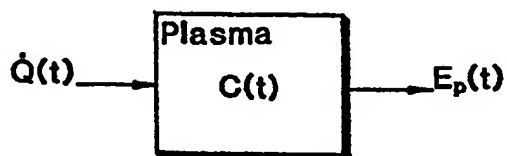


FIG. 3.

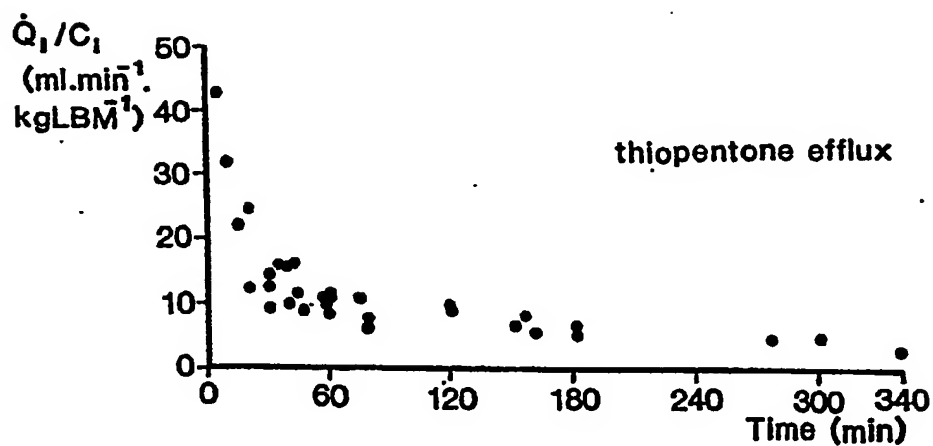


FIG. 4.

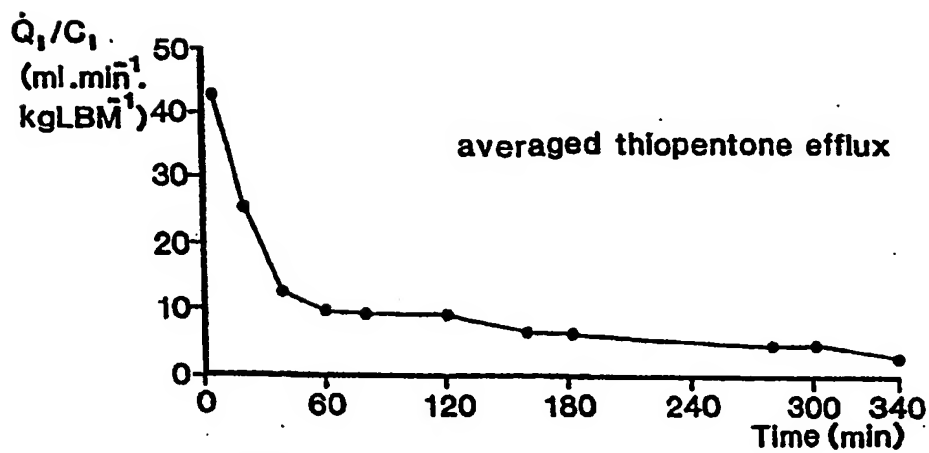
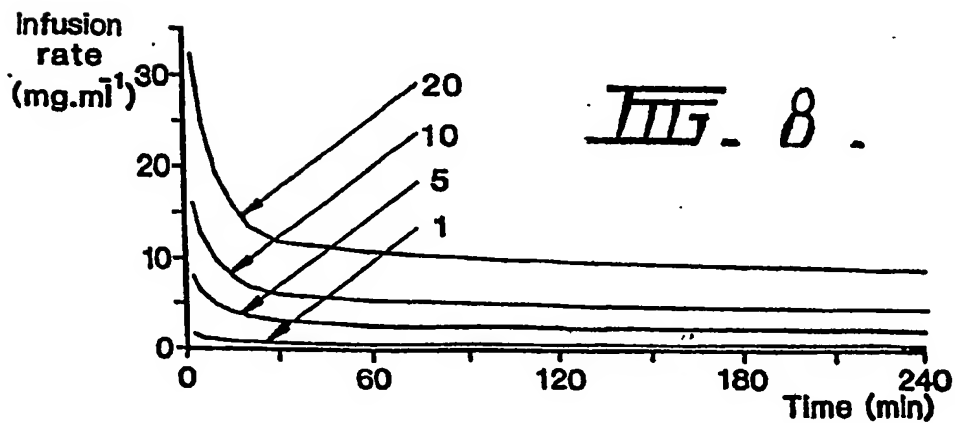
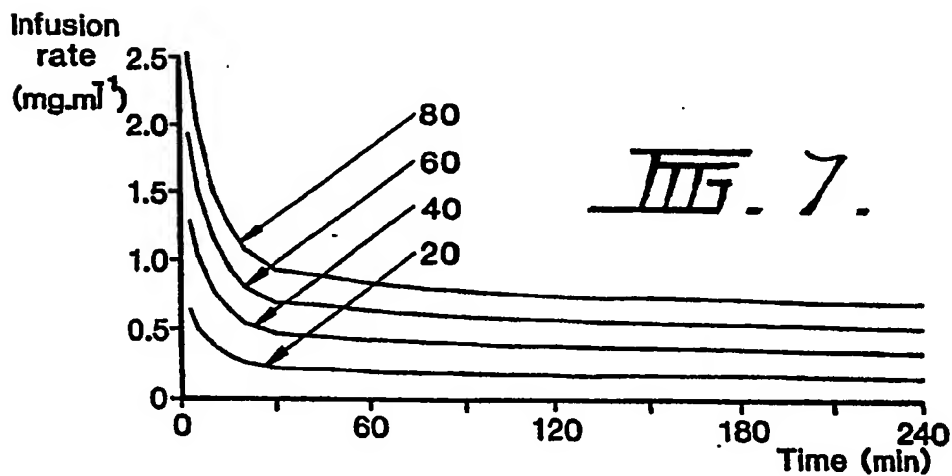
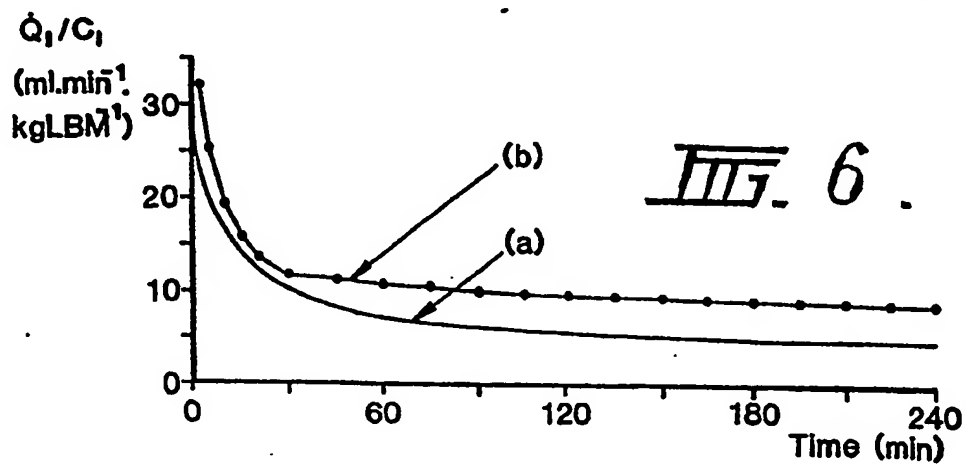


FIG. 5.



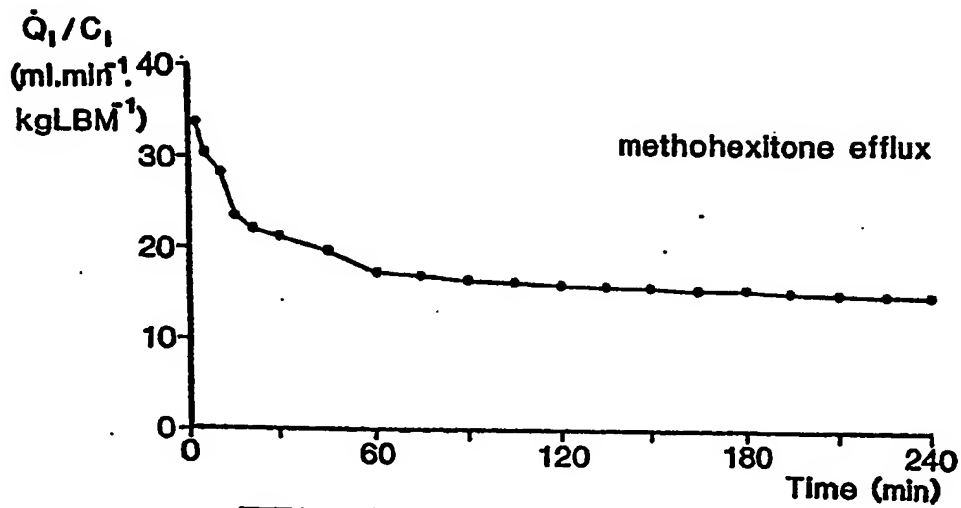
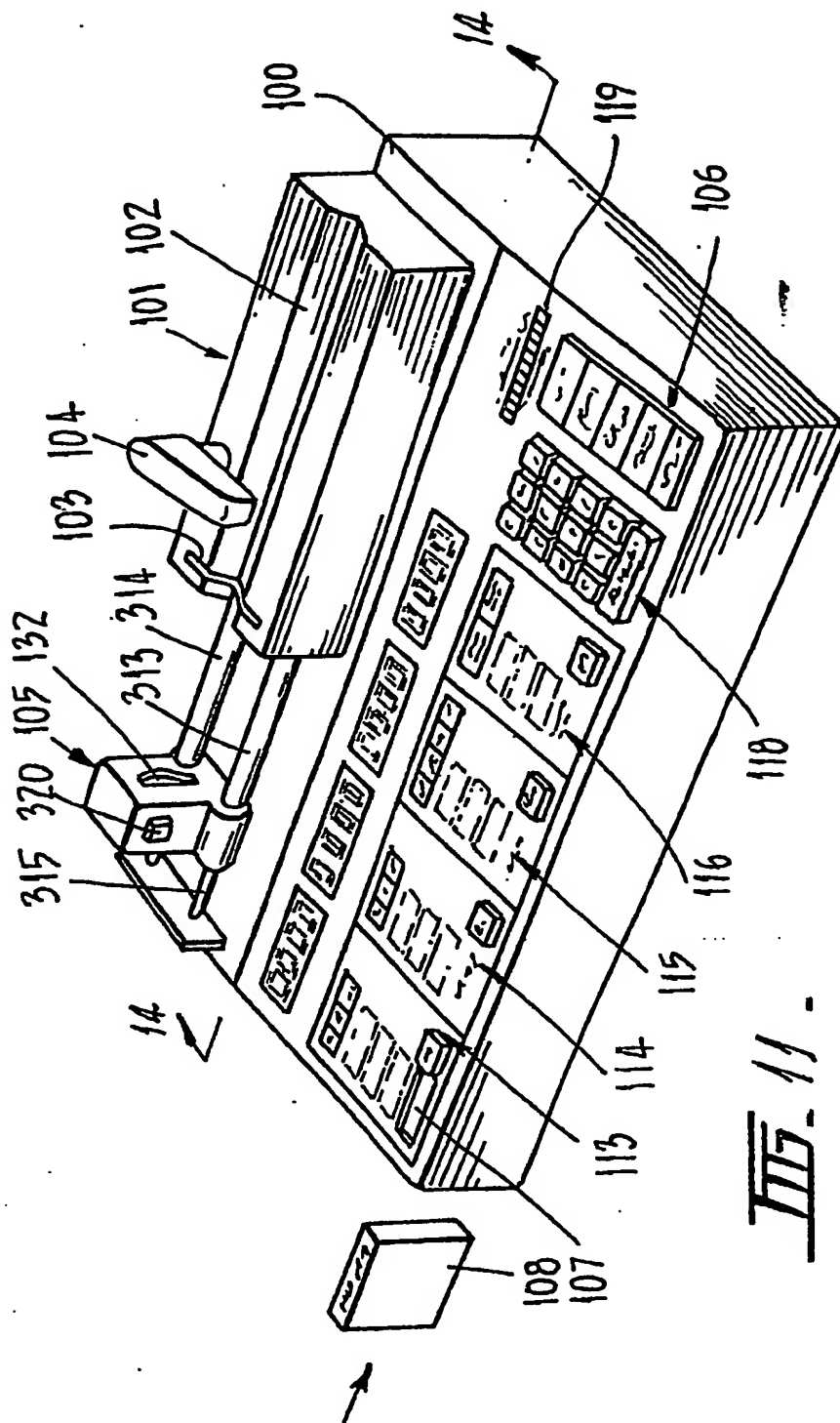


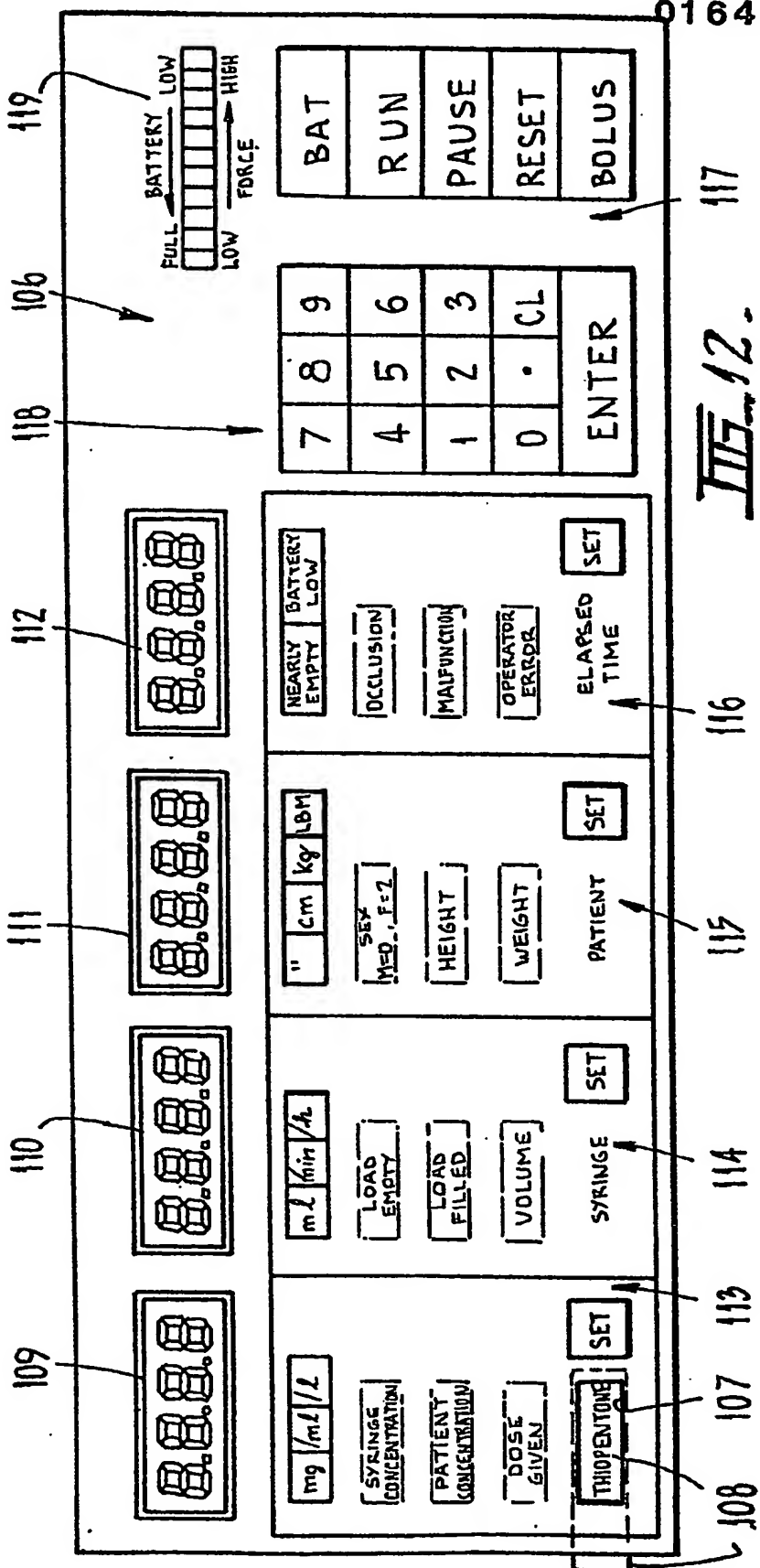
FIG. 9.



FIG. 10.



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7/11

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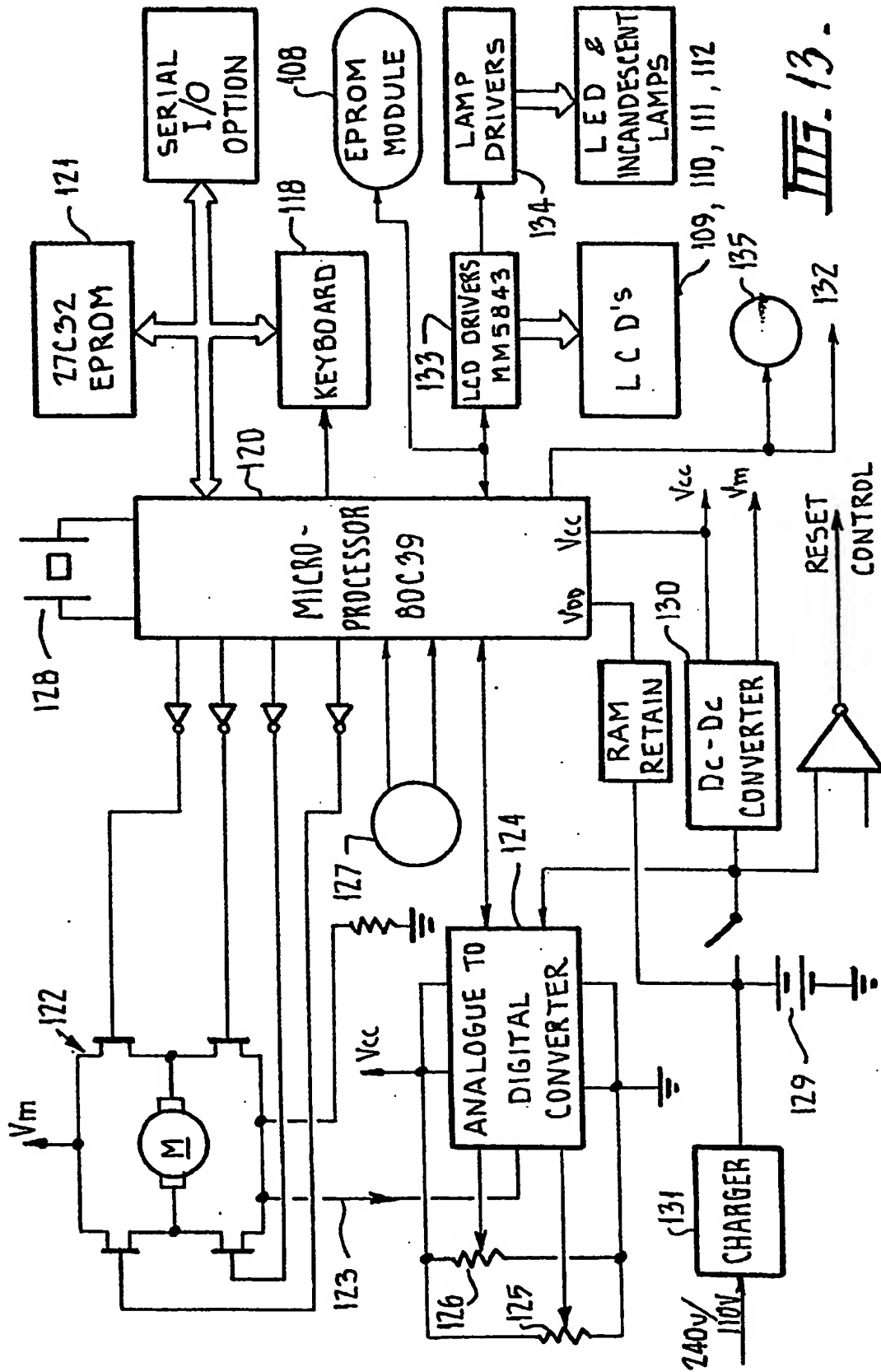
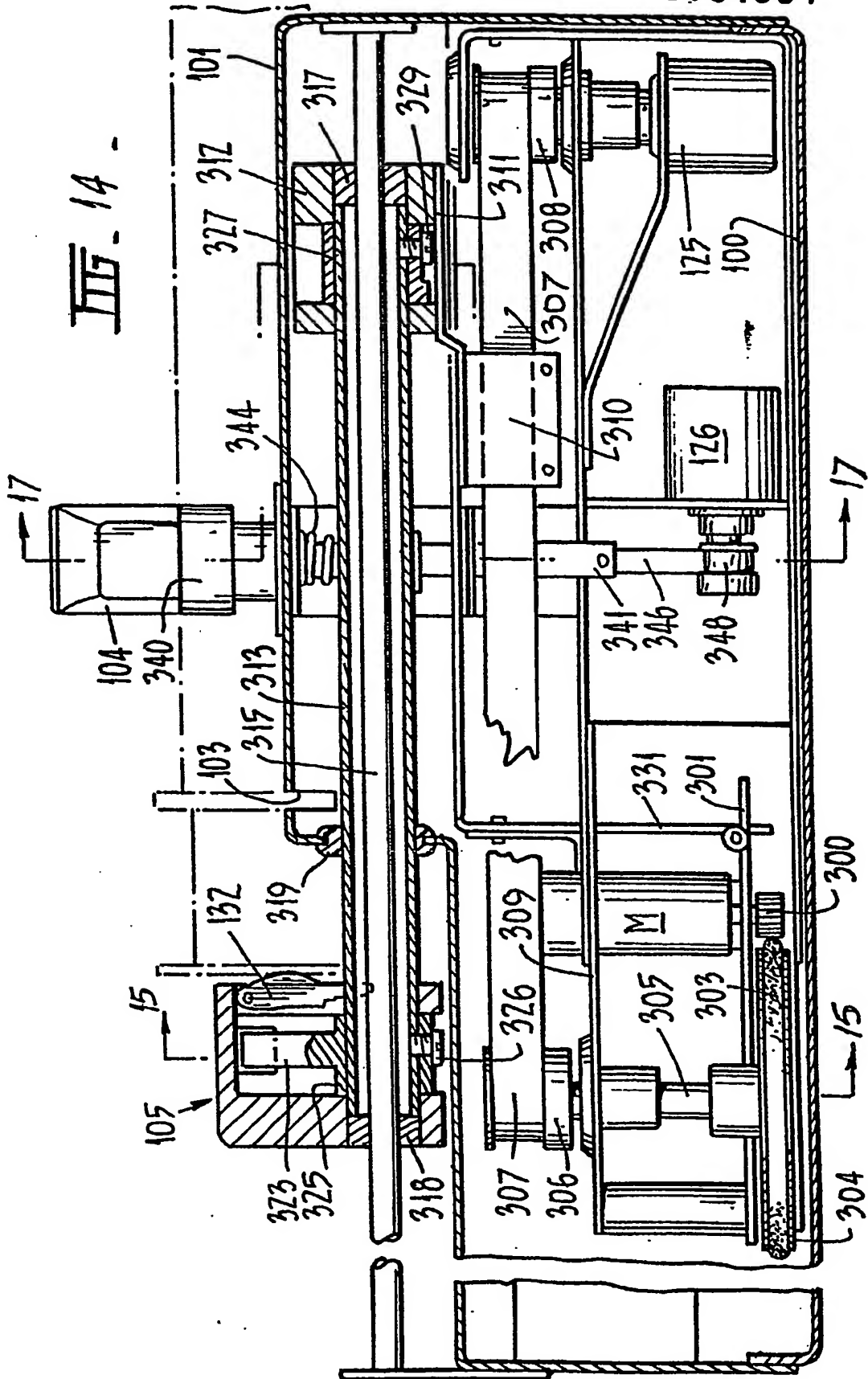
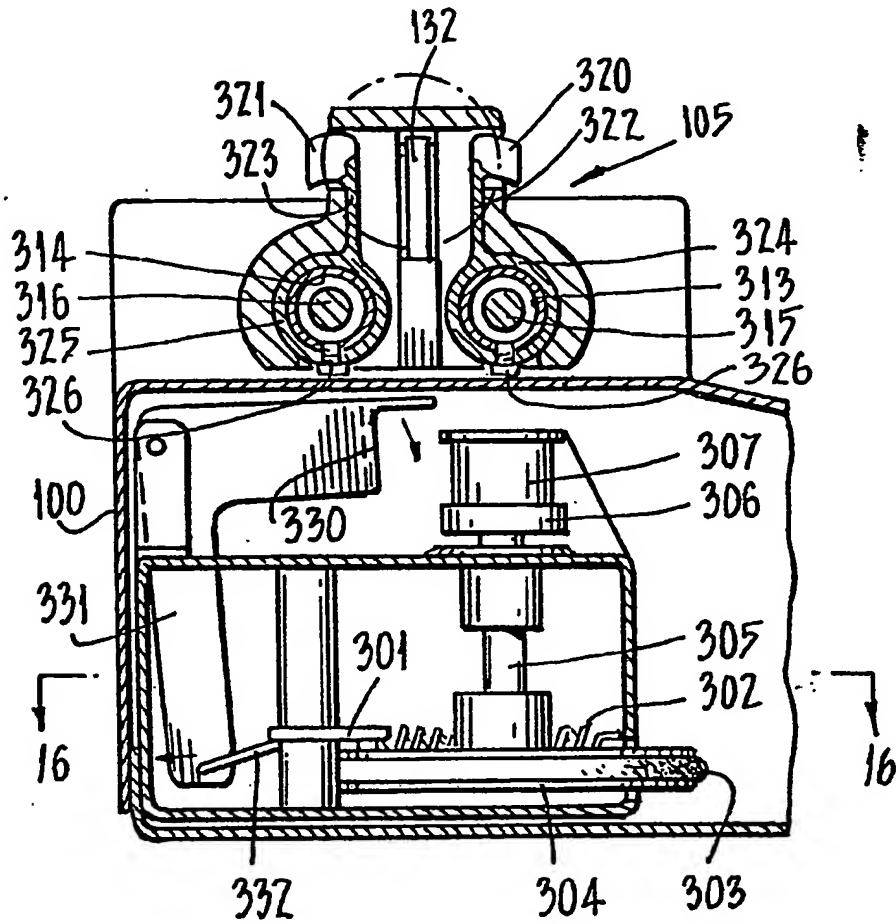
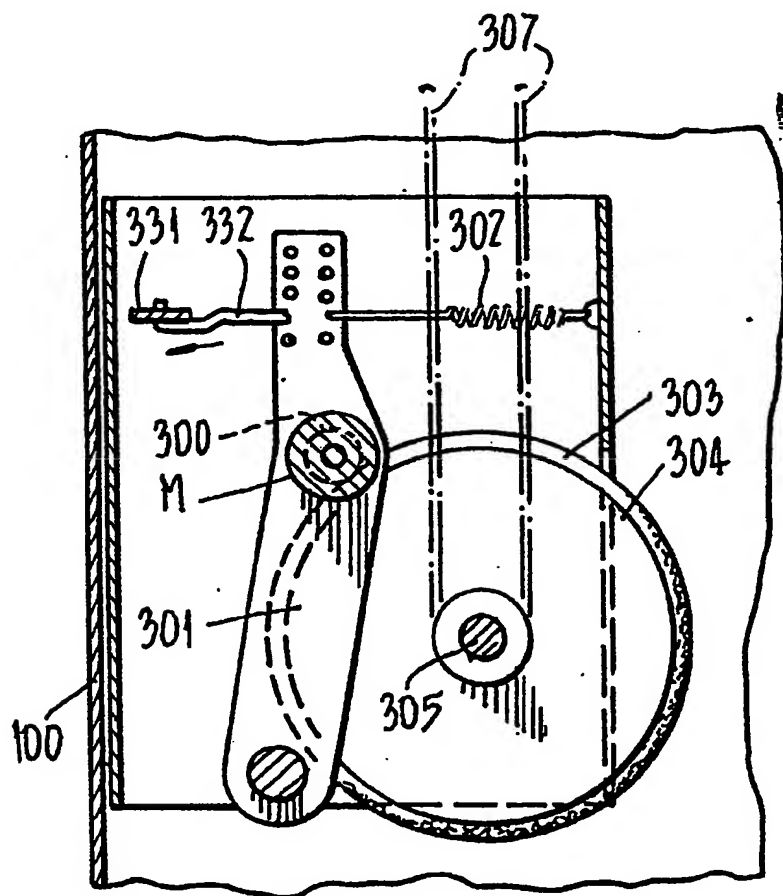


FIG. 13.



FIG. 15.

FIG. 16.